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Chemical polysialylation and in vivo tetramerization improve pharmacokinetic characteristics of recombinant human butyrylcholinesterase-based bioscavengers

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Abstract

© 2015 Park-media, Ltd. Organophosphate toxins (OPs) are the most toxic low-molecular compounds. The extremely potent toxicity of OPs is determined by their specificity toward the nerve system. Human butyrylcholinesterase (hBChE) is a natural bioscavenger against a broad spectrum of OPs, which makes it a promising candidate for the development of DNA-encoded bioscavengers. The high values of the protective index observed for recombinant hBChE (rhBChE) make it appropriate for therapy against OP poisoning, especially in the case of highly toxic warfare nerve agents. Nevertheless, large-scale application of biopharmaceuticals based on hBChE is restricted due to its high cost and extremely rapid elimination from the bloodstream. In the present study, we examine two approaches for long-acting rhBChE production: I) chemical polysialylation and II) in-vivo tetramerization. We demonstrate that both approaches significantly improve the pharmacokinetic characteristics of rhBChE (more than 5 and 10 times, respectively), which makes it possible to use rhBChE conjugated with polysialic acids (rhBChE-CAO) and tetrameric rhBChE (4rhBChE) in the treatment of OP poisonings.

Keywords

Biodistribution, Biopharmaceutical, Bioscavenger, Butyrylcholinesterase, In vivo tetramerization, Pharmacokinetics, Polysialylation